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Substitute for form 1449A/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use as many sheets as necessary)	Complete if Known	
	Application Number	10/753,665
	Filing Date	January 8, 2004
	First Named Inventor	Carson, Dennis
	Group Art Unit	1614
	Examiner Name	Krass, Frederick
Sheet 1 of 2		Attorney Docket No: 103.014US3



US PATENT DOCUMENTS				
Examiner Initial.*	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Filing Date If Appropriate
FK	US-2002/0042375A1	04/11/2002	Heimbrook, D. C., et al.	06/29/2001
	US-2003/0004142A1	01/02/2003	Prior, C. P., et al.	04/17/2002
	US-2003/0004143A1	01/02/2003	Prior, C. P., et al.	04/18/2002
	US-3,053,255	09/11/1962	Meyer, Friedrich	12/16/1958
	US-3,710,795	01/16/1973	Higuchi, Takeru, et al.	09/29/1970
	US-3,843,480	10/22/1974	Dreher, Donald F.	12/04/1967
	US-3,939,178	02/17/1976	Demerson, Christopher A., et al.	09/15/1972
	US-3,948,254	04/06/1976	Zaffaroni, Alejandro	08/28/1974
	US-3,948,262	04/06/1976	Zaffaroni, Alejandro	03/10/1975
	US-3,974,179	08/10/1976	Demerson, Christopher A., et al.	10/10/1974
	US-3,993,073	11/23/1976	Zaffaroni, Alejandro	03/03/1975
	US-4,310,509	01/12/1982	Berglund, Claire A., et al.	07/31/1979
	US-4,460,562	07/17/1984	Keith, Alec D., et al.	03/30/1983
	US-4,466,953	08/21/1984	Keith, Alec D., et al.	09/30/1982
	US-4,482,534	11/13/1984	Blank, Izhak	08/18/1983
	US-4,485,097	11/27/1984	Bell, E.	05/25/1983
	US-4,505,891	03/19/1985	Ito, Toshio	
	US-4,533,540	08/06/1985	Blank, Izhak	08/30/1984
	US-4,542,012	08/17/1985	Dell, John D.	02/11/1983
	US-4,542,013	09/17/1985	Keith, Alec D., et al.	08/16/1983
	US-4,560,555	12/24/1985	Snider, Bruno	12/12/1983
	US-4,585,877	04/29/1986	Demerson, Christopher A., et al.	05/06/1985
	US-4,597,961	07/01/1986	Etscorn, Frank T.	01/23/1985
	US-4,608,249	08/26/1986	Otsuka, Saburo	11/02/1982
	US-4,686,213	08/11/1987	Ferdinandi, Eckhardt S., et al.	08/15/1986
	US-4,748,252	05/31/1988	Ferdinandi, Eckhardt S., et al.	01/28/1987
	US-4,806,356	02/21/1989	Shaw, Alec S.	04/03/1987
	US-4,940,587	07/10/1990	Jenkins, Anthony W., et al.	06/03/1986
	US-5,599,946	02/04/1997	Vincenzo, Giobbio, et al.	05/30/1995
	US-5,776,967	07/07/1998	Kreft, Anthony F., et al.	07/07/1997
	US-5,824,699	10/20/1998	Kreft, Anthony F., et al.	03/16/1998
	US-5,939,455	08/17/1999	Rephaeli, Ada	03/11/1997
	US-5,968,974	10/19/1999	Kargman, Stacia, et al.	10/10/1997
	US-5,981,592	11/09/1999	Wechter, W. J., et al.	04/09/1998
	US-6,160,018	12/12/2000	Wechter, William J., et al.	03/10/1997
FK	US-6,545,034	04/01/2003	Carson, et al.	07/23/1999

EXAMINER

Krass, Frederick

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Sheet 2 of 2

Attorney Docket No: 103.014US3

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	T <sup>2</sup>
FK	WO-0106990A2	02/01/2001	Carson, Dennis A.	
	WO-0212188A2	02/14/2002	Carson, Dennis A.	
↓	WO-9748391A3	12/24/1997	Xiaotao, Quian	
FK	WO-98/40078A1	09/17/1998	Rephaeli, A.	

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
FK		HEATH, CLARK W., "Nonsteroidal Antiinflammatory Drugs and Human Cancer", American Cancer Society, Volume 74, Number 10, (November 15, 1994), 2885-2886	
		LEMAN, EDDY S., et al., "Characterization of the Nuclear Matrix Proteins in a Transgenic Mouse Model for Prostate Cancer", Journal of Cellular Biochemistry, 86, (2002), 203-212	
		MCCRACKEN, JOHN D., "Antiproliferative Effects of the Enantiomers of Flurbiprofen", Journal of Clinical Pharmacology, (1996), 540-545	
		PIAZZA, GARY A., "Apoptosis Primarily Accounts for the Growth-inhibitory Properties of Sulindac Metabolites and Involves a Mechanism That is Independent of Cyclooxygenase Inhibition, Cell Cycles Arrest, and p53 Induction", Cancer Research, Volume 57, (June 15, 1997), 2452-2459	
		RILEY, et al., "New Drugs: a six month review", US Pharmacist, Vol. 16, (September 1991), 35-64	
		THUN, MICHAEL J., "Aspirin, NSAIDs, and digestive tract cancers", Cancer and Metastasis Reviews 13, Kluwer Academic Publishers., (1994), 269-277	
		WECHTER, WILLIAM J., "R-Flurbiprofen (E-7869), a chemopreventive and treatment of cancer", Inflammopharmacology, Volume 8, No. 2, (2000), 189-206	
		WECHTER, WILLIAM J., "R-Flurbiprofen Chemoprevention and Treatment of Intestinal Adenomas in the APC min/+ Mouse Model: Implications for Prophylaxis and Treatment of Colon Cancer", Cancer Research, Volume 57, Number 19, (October 1, 1997), 4316-4324	
FK		WECHTER, WILLIAM J., "Rac-Flurbiprofen Is More Ulcerogenic Than Its (S)-Enantiomer", Chirality, Volume 5, Number 7, (1993), 492-494	

EXAMINER

Krass, Frederick

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Substitute Disclosure Statement Form (PTO-1449)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

1/8/2004

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	Group Art Unit	Unknown /614
	Examiner Name	Krass, Frederick
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## US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
FK	US-3,843,681	10/22/1974	Demerson, C. A., et al.	260	326.14 R	06/01/1971
	US-4,337,760	07/06/1982	Rubin, D.	128	1 R	10/31/1979
	US-5,561,151	10/01/1996	Young, J. W., et al.	514	411	01/04/1995
	US-5,811,558	09/22/1998	Adger, B. M., et al.	548	427	04/11/1995
FK	US-5,955,504	09/21/1999	Wechter, William J., et al.	514	568	03/13/1995

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T <sup>2</sup>
FK	DE-2226340	03/15/1973	Demerson, Christopher A., et al.	C07 D	27/56	
	EP-0289262	11/02/1986	Venuti, M. C., et al.	C07 C	93/00	
	WO-00/02555	01/20/2000	Nardella, Francis A., et al.	A61K	31/40	
	WO-00/13410	03/09/2000	Monroe, D. A.	H04 N	5/76	
	WO-96/28148	09/19/1996	Wechter, William J., et al.	A61K	31/19	
	WO-98/09603	03/12/1998	Wechter, William J., et al.	A61K		
FK	WO-98/18490	05/07/1998	Clynes, M. M.	A61K	45/06	

## OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

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FK		The Merck Index, Eleventh Edition, Budavari, S., et al., (eds.), Merck & Co., Inc., Rahway, N.J., Entry No. 3831 -- "Etodolac", (1989), p. 608	
		In: Remington's Pharmaceutical Sciences, Eighteenth Edition, Gennaro, A.R., (ed.), Mack Publishing Company, Easton, PA, (1990), pp. 1115-1121	
		ABRAMSON, S. B., et al., "The Mechanisms of Action of Nonsteroidal Antiinflammatory Drugs", Arthritis & Rheumatism, 32 (1), (Jan. 1989), pp. 1-9	
		ALEXANIAN, R., et al., "The Treatment of Multiple Myeloma", The New England Journal of Medicine, 330 (7), (Feb. 17, 1994), pp. 484-489	
		BARLOGIE, B., et al., "Prognostic Factors with High-Dose Melphalan for Refractory Multiple Myeloma", Blood, 72, (1988), 2015-2019	
		BATAILLE, R., et al., "Multiple Myeloma", New England Journal of Medicine, 336, (1997), 1657-1664	
FK		BECKER-SCHARFENKAMP, U., et al., "Evaluation of the Stereoselective Metabolism of the Chiral Analgesic Drug Etodolac by High-Performance Liquid Chromatography", Journal of Chromatography, 621 (2), (Nov. 24, 1993), pp. 199-	

EXAMINER

Krass, Frederick

DATE CONSIDERED

12-21-04

Substitute Disclosure Statement Form (PTO-1448)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. † Applicant's unique citation designation number (optional) ‡ Applicant is to place a check mark here if English language translation is attached

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	Examiner Name	Krass, Frederick
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FK		207	
		BELLOSILLO, B. , et al., "Aspirin and Salicylate Induce Apoptosis and Activation of Caspases in B-Cell Chronic Lymphocytic Leukemia Cells", <u>Blood</u> , 92 (4), (Aug. 15, 1998),pp. 1406-1414	
		BERENDES, U. , et al., "Simultaneous Determination of the Phase II Metabolites of the Non Steroidal Anti-inflammatory Drug Etodolac in Human Urine", <u>Enantiomer</u> , 1, Abstract Only, Chemical Abstracts, Abstract No. 126:207064q,(1996),415-422	
		BRENNA, E. , et al., "New Enzymatic and Chemical Approaches to Enantiopure Etodolac", <u>Tetrahedron</u> , 53, (1997),17769-17780	
		BROCKS, D. R., et al., "Etodolac Clinical Pharmacokinetics", <u>Clinical Pharmacokinetics</u> , 26 (4), (1994),pp. 259-274	
		CARSON, D. A., et al., "Oral Antilymphocyte Activity and Induction of Apoptosis by 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine", <u>Proc. Natl. Acad. Sci. USA</u> , 89 (7), (Apr. 1992),pp. 2970-2974	
		CHINETTI, G. , et al., "Activation of Proliferator-activated Receptors alpha and Y Induces Apoptosis of Human Monocyte-derived Macrophages", <u>The Journal of Biological Chemistry</u> , 273 (40), (Oct. 2, 1998),pp. 25573-25580	
		CUNNINGHAM, D , et al., "High-dose Melphalan for Multiple Myeloma: Long-term Follow-up Data", <u>Journal of Clinical Oncology</u> , 12, (1994),764-768	
		DEMERSON, C. A., et al., "Etodolic Acid and Related Compounds. Chemistry and Antiinflammatory Actions of Some Potent Di- and Trisubstituted 1,3,4,9-Tetrahydropyrano[3,4-b]indole-1-acetic Acids", <u>Journal of Medicinal Chemistry</u> , 19 (3), (1976),pp. 391-395	
		DEMERSON, C. A., et al., "Resolution of Etodolac and Antiinflammatory and Prostaglandin Synthetase Inhibiting Properties of the Enantiomers", <u>J. Med. Chem.</u> , 26 (12), (Dec. 1983),pp. 1778-1780	
		DRACHENBERG, D. E., "Treatment of Prostate Cancer: Watchful Waiting, Radical Prostatectomy, and Cryoablation", <u>Seminars in Surgical Oncology</u> , 18 (1), (Jan/Feb. 2000),pp. 37-44	
		DUFFY, C. P., et al., "Enhancement of Chemotherapeutic Drug Toxicity to Human Tumour Cells In Vitro by a Subset of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)", <u>European Journal of Cancer</u> , 34 (8), (July 1998),pp. 1250-1259	
		HAHNFELD, L. E., et al., "Prostate Cancer", <u>The Medical Clinics of North America - The Aging Male Patient</u> , 83 (5), (Sept. 1999),pp.1231-1245	
		HAROUSSEAU, J. L., et al., "Double-Intensive Therapy in High-Risk Multiple Myeloma", <u>Blood</u> , 79 (11), (June 1, 1992),pp. 2827-2833	
V		KRAJEWSKI, S. , et al., "Detection of Multiple Antigens on Western Blots", <u>Analytical Biochemistry</u> , 236 (2), Article No. 0160,(May 1996),pp. 221-228	
FK		LANDIS, S. H., et al., "Cancer Statistics, 1998", <u>CA Cancer J. Clin.</u> , 48 (1),	

EXAMINER

Krass, Frederick

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12-21-04

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Application Number	Unknown 10/753 665
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First Named Inventor	Carson, Dennis
Group Art Unit	Unknown 16/14
Examiner Name	Krass, Frederick

Sheet 3 of 4

Attorney Docket No: 103.014US3

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T*
FK		(1998), pp. 6-29	
		LEE, D. H., "Proteasome Inhibitors: Valuable New Tools For Cell Biologists", <u>Trends in Cell Biology</u> , 8, (October 1998), pp. 397-403	
		LEHMANN, J. M., et al., "Peroxisome Proliferator-activated Receptors alpha and Y Are Activated by Indomethacin and Other Non-steroidal Anti-inflammatory Drugs", <u>The Journal of Biological Chemistry</u> , 272 (6), (Feb. 7, 1997), pp. 3406-3410	
		LEONI, L. M., et al., "Induction of an Apoptotic Program in Cell-Free Extracts by 2-Chloro-2'-deoxyadenosine 5'-triphosphate and Cytochrome C", <u>PNAS, USA</u> , 95 (16), (Aug. 4, 1998), pp. 9567-9571	
		LOCHMULLER, C. H., et al., "Chromatographic Resolution of Enantiomers -- Selective Review", <u>Journal of Chromatography</u> , 113 (3), (Oct. 22, 1975), pp. 283-302	
		MARTEL, R. R., et al., "Anti-inflammatory and Analgesic Properties of Etodolic Acid in Rats", <u>Canadian Journal of Physiology and Pharmacology</u> , 54 (3), (June 1976), pp. 245-248	
		MOONEY, P. T., et al., "Cell Pathways' Exisulind 'Aptosyn' Demonstrates Potential to Delay Hormone Therapy in Post-Prostatectomy Men at Risk of Prostate Cancer Recurrence", <a href="http://biz.yahoo.com/bw/000501/ga_cell_pa_1.html">http://biz.yahoo.com/bw/000501/ga_cell_pa_1.html</a> , (May 2000), 3 p.	
		NARDELLA, FRANCIS A., et al., "Enhanced Clearance of Leukemic Lymphocytes in B Cell Chronic Lymphocytic Leukemia (CLL) with Etodolac", <u>Arthritis &amp; Rheumatism</u> , 42 (9) Supplement, Abstract No. 41, (Sept. 1999), p. S56	
		RICOTE, M., et al., "The Peroxisome Proliferator-Activated Receptor-Y is a Negative Regulator of Macrophage Activation", <u>Nature</u> , 391, (Jan. 1, 1998), pp. 79-82	
		RIEDEL, D. A., et al., "The Epidemiology of Multiple Myeloma", <u>Hematology/Oncology Clinics of North America</u> , Multiple Myeloma, 6 (2), (April 1992), pp. 225-247	
		ROYALL, J. A., et al., "Evaluation of 2',7'-Dichlorofluorescein and Dihydrorhodamine 123 as Fluorescent Probes for Intracellular H2O2 in Cultured Endothelial Cells", <u>Archives of Biochemistry and Biophysics</u> , 302 (2), (May 1, 1993), pp. 348-355	
		SHIFF, S. J., et al., "Nonsteroidal Antiinflammatory Drugs Inhibit the Proliferation of Colon Adenocarcinoma Cells: Effects on Cell Cycle and Apoptosis", <u>Experimental Cell Research</u> , 222, Article No. 0023, (1996), pp. 179-188	
✓		TANG, D. G., et al., "Target to Apoptosis: A Hopeful Weapon for Prostate Cancer", <u>The Prostate</u> , (1997), pp. 284-293	
FK		VAN BREEMEN, R. B., et al., "Characterization of Oxygen-Linked Glucuronides by Laser Desorption Mass Spectrometry", <u>Biomed. Mass Spectrom.</u> , 11, Abstract	

EXAMINER

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FL		Only, Chemical Abstracts, Abstract No. 101:106777c,(1984),278-283	
		VENUTI, M. C., et al., "Synthesis and Biological Evaluation of omega-(N,N,N-trialkylammonium)alkyl Esters and Thioesters of Carboxylic Acid Nonsteroidal Antiinflammatory Agents", <u>Pharm. Res.</u> , 6, Abstract Only, Chemical Abstracts, Abstract No. 112:111681y,(1989),867-873	
		WANG, X. , et al., "Antipoptotic Action of 1,25-Dihydroxyvitamin D3 Is Associated with Increased Mitochondrial MCL-1 and RAF-1 Proteins and Reduced Release of Cytochrome c", <u>Experimental Cell Research</u> , 235 (1), Article No. EX973667,(1997),pp. 210-217	
		WECHTER, W. J., et al., "E-7869 (R-Flurbiprofen) Inhibits Progression of Prostate Cancer in the TRAMP Mouse", <u>Cancer Research</u> , 60, (April 15, 2000),pp. 2203-2208	
		WEISS, H. A., et al., "Aspirin, Non-Steroidal Anti-Inflammatory Drugs and Protection from Colorectal Cancer: a Review of the Epidemiological Evidence", <u>Scandinavian Journal of Gastroenterology</u> , 31 (Suppl. 220), (1996),pp. 137-141	
FL		WILEN, S. H., et al., "Strategies In Optical Resolutions", <u>Tetrahedron</u> , 33 (21), Tetrahedron Report Number 38,(1977),pp. 2725-2736	

EXAMINER

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